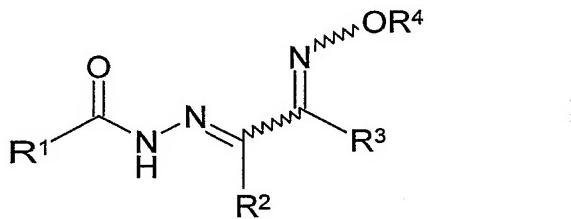


AMENDED CLAIMS

[received by the International Bureau on 08 August 2005 (08.08.05);
original claims 1 – 36 replaced by amended claims 1 – 37 (15 pages)]

1. A use of a compound of formula I,



5

wherein

the squiggly bonds represent optional *E* or *Z* geometry;

10

R¹ and R² independently represent an aryl group or a heteroaryl group, both of which groups are optionally substituted by one or more substituents selected from:

X¹, C₁₋₈ alkyl, an aryl group and a heterocyclic group:-

15 (A) which C₁₋₈ alkyl group is itself optionally substituted by one or more Z substituents; and

(B) which C₁₋₈ alkyl, aryl and heterocyclic groups may themselves be substituted by one or more substituents selected from X¹, C₁₋₈ alkyl (which latter group may be further substituted by one or more substituents selected from X¹, C₁₋₈ alkyl, an aryl group, a heterocyclic group and Z), an aryl group and a heterocyclic group (and which latter two groups may be further substituted by one or more substituents selected from X¹, C₁₋₈ alkyl, an aryl group and a heterocyclic group), in which:-

20 25 X¹ represents, on each occasion when used above, halo, cyano, -N₃, -NO₂, -ONO₂ or -A¹-R⁵, wherein:

A¹ represents a spacer group selected from -C(Z)A²-, -N(R⁶)A³-, -OA⁴-, -S- or -S(O)_nA⁵-, in which:

A² represents a single bond, -O-, -S-, -N(R⁶)A⁶- or -C(Z)-;

A³ represents A⁶, -C(Z)N(R⁶)C(Z)N(R⁶)-, -C(Z)N(R⁶)C(Z)O-, -C(Z)N(R⁶)S(O)_nN(R⁶)-, -C(Z)S-, -S(O)_n-, -S(O)_nN(R⁶)C(Z)N(R⁶)-, -S(O)_nN(R⁶)C(Z)O- or -S(O)_nN(R⁶)S(O)_nN(R⁶)-;

A⁴ represents A⁶ or -S(O)_n;

A⁵ represents a single bond, -N(R⁶)- or -O-;

A⁶ represents, on each occasion when used above, a single bond, -C(Z)-,

10 -C(Z)O-, -C(Z)N(R⁶)-, -S(O)_nN(R⁶)- or -S(O)_nO-; and

Z represents, on each occasion when used above, a substituent connected by a double bond, which is selected from =O, =S, =NR⁵, =NN(R⁵)(R⁶), =NOR⁵, =NS(O)₂N(R⁵)(R⁶), =NCN, =C(H)NO₂ and =C(R⁵)(R⁶);

15

R⁵ and R⁶ independently represent, on each occasion when used above,

(a) hydrogen;

(b) C₁₋₈ alkyl, optionally substituted by one or more substituents selected from X², Q, C₁₋₈ alkyl (optionally substituted by one or more substituents selected from X², C₁₋₈ alkyl, an aryl group, a heterocyclic group and Q), an aryl group and a heterocyclic group (which latter two groups are optionally substituted by one or more substituents selected from X², C₁₋₈ alkyl, an aryl group and a heterocyclic group); or

20 (c) an aryl group or a heterocyclic group, both of which are optionally substituted by one or more substituents selected from X², C₁₋₈ alkyl (optionally substituted by one or more substituents selected from X², C₁₋₈ alkyl, an aryl group, a heterocyclic group and Q), an aryl group and a heterocyclic group (which latter two groups are optionally

substituted by one or more substituents selected from X^2 , C_{1-8} alkyl, an aryl group and a heterocyclic group); or

R^5 and R^6 may, when present on the same atom or on adjacent atoms, taken together with those atoms form a 5- to 8-membered ring optionally containing 1 to 3 heteroatoms and/or 1 to 3 double bonds, which ring is itself optionally substituted by one or more substituents selected from X^2 , C_{1-8} alkyl, an aryl group, a heterocyclic group (which latter three groups are optionally substituted as described in (b) and (c) above, respectively) and, provided that the ring that R^5 and R^6 may together be part of is not aromatic in character, Q;

X^2 represents, on each occasion when used above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^7-R^7$, wherein:

A^7 represents a spacer group selected from $-C(Q)A^8-$, $-N(R^8)A^9-$, $-OA^{10}-$, $-S-$ or $-S(O)_nA^{11}-$, in which:

A^8 represents a single bond, $-O-$, $-S-$, $-N(R^8)-$ or $-C(Q)-$;

A^9 represents A^{12} , $-C(Q)N(R^8)C(Q)N(R^8)-$, $-C(Q)N(R^8)C(Q)O-$, $-C(Q)N(R^8)S(O)_nN(R^8)-$, $-C(Q)S-$, $-S(O)_n-$, $-S(O)_nN(R^8)C(Q)N(R^8)-$, $-S(O)_nN(R^8)C(Q)O-$ or $-S(O)_nN(R^8)S(O)_nN(R^8)-$;

A^{10} represents A^{12} or $-S(O)_n-$;

A^{11} represents a single bond, $-N(R^8)-$ or $-O-$;

A^{12} represents, on each occasion when used above, a single bond, $-C(Q)-$, $-C(Q)O-$, $-C(Q)N(R^8)-$, $-S(O)_nN(R^8)-$ or $-S(O)_nO-$;

Q represents, on each occasion when used above, a substituent connected by a double bond, which is selected from $=O$, $=S$, $=NR^7$, $=NN(R^7)(R^8)$, $=NOR^7$, $=NS(O)_2N(R^7)(R^8)$, $=NCN$, $=C(H)NO_2$ and $=C(R^7)(R^8)$;

R^7 and R^8 independently represent, on each occasion when used herein,

(i) hydrogen;

(ii) an aryl group or a heterocyclic group, both of which may be substituted by one or more substituents selected from X^3 , C_{1-8} alkyl, an aryl group and a heterocyclic group (and which latter three groups are themselves optionally substituted by one or more substituents selected from halo, hydroxy, $-R^9$, $-OR^9$ and, provided that the group is not aromatic in nature, $=O$); or

(iii) C_{1-8} alkyl, optionally substituted by one or more substituents selected from X^3 and W ; or

R^7 and R^8 may, when present on the same atom or on adjacent atoms, taken together with those atoms form a 5- to 8-membered ring optionally containing 1 to 3 heteroatoms and/or 1 to 3 double bonds, which ring is itself optionally substituted by one or more substituents selected from X^3 , C_{1-8} alkyl, an aryl group, a heterocyclic group and, provided that the ring that R^7 and R^8 may together be part of is not aromatic in character, W ;

15

X^3 represents, on each occasion when used above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^{13}-R^{10}$, wherein:

A^{13} represents a spacer group selected from $-C(W)A^{14}-$, $-N(R^{11})A^{15}-$, $-OA^{16}-$, $-S-$ or $-S(O)_nA^{17}-$, in which:

20 A^{14} represents a single bond, $-O-$, $-S-$, $-N(R^{11})-$ or $-C(W)-$;

A^{15} represents A^{18} , $-C(W)N(R^{11})C(W)N(R^{11})-$, $-C(W)N(R^{11})C(W)O-$, $-C(W)N(R^{11})S(O)_nN(R^{11})-$, $-C(W)S-$, $-S(O)_n-$, $-S(O)_nN(R^{11})C(W)N(R^{11})-$, $-S(O)_nN(R^{11})C(W)O-$ or $-S(O)_nN(R^{11})S(O)_nN(R^{11})-$;

A^{16} represents A^{18} or $-S(O)_n-$;

25 A^{17} represents a single bond, $-N(R^{11})-$ or $-O-$;

A^{18} represents, on each occasion when used above, a single bond, $-C(W)-$, $-C(W)O-$, $-C(W)N(R^{11})-$, $-S(O)_nN(R^{11})-$ or $-S(O)_nO-$;

30 R^9 represents, on each occasion when used above, C_{1-6} alkyl optionally substituted by one or more fluorine atoms;

W represents, on each occasion when used above, a substituent connected by a double bond, which is selected from =O, =S, =NR¹⁰, =NN(R¹⁰)(R¹¹), =NOR¹⁰, =NS(O)₂N(R¹⁰)(R¹¹), =NCN, =C(H)NO₂ and =C(R¹⁰)(R¹¹);

5

R¹⁰ and R¹¹ independently represent, on each occasion when used above:

- (1) hydrogen;
- (2) an aryl group or a heterocyclic group, both of which may be substituted by one or more substituents selected from X⁴, C₁₋₈ alkyl, methylenedioxy, difluoromethylenedioxy and dimethylmethylenedioxy; or
- (3) C₁₋₈ alkyl, optionally substituted by one or more substituents selected from X⁴, =O, =S, =NR¹², =NN(R¹²)(R¹³), =NOR¹², =NS(O)₂N(R¹²)(R¹³), =NCN, =C(H)NO₂ and =C(R¹²)(R¹³); or

R¹⁰ and R¹¹ may, when present on the same atom or on adjacent atoms, taken together with those atoms form a 5- to 8-membered ring optionally containing 1 to 3 heteroatoms and/or 1 to 3 double bonds, which ring is itself optionally substituted by one or more substituents selected from X⁴ and, provided that the ring that R¹⁰ and R¹¹ may together be part of is not aromatic in character, =O, =S, =NR¹², =NN(R¹²)(R¹³), =NOR¹², =NS(O)₂N(R¹²)(R¹³), =NCN, =C(H)NO₂ and =C(R¹²)(R¹³);

X⁴ represents, on each occasion when used above, halo, cyano, -N₃, -NO₂, -ONO₂ or -A¹⁹-R¹², wherein:

A¹⁹ represents a spacer group selected from -C(O)A²⁰-, -N(R¹³)A²¹-, -OA²²-, -S- or -S(O)_nA²³-, in which:

A²⁰ represents a single bond, -O-, -S-, -N(R¹³)- or -C(O)-;

A²¹ represents A²⁴, -C(O)N(R¹³)C(O)N(R¹³)-, -C(O)N(R¹³)C(O)O-, -C(O)N(R¹³)S(O)_nN(R¹³)-, -C(O)S-, -S(O)_n-, -S(O)_nN(R¹³)C(O)N(R¹³)-, -S(O)_nN(R¹³)C(O)O- or -S(O)_nN(R¹³)S(O)_nN(R¹³)-;

A²² represents A²⁴ or -S(O)_n-;

A²³ represents a single bond, -N(R¹³)- or -O-;

A²⁴ represents, on each occasion when used above, a single bond, -C(O)-, -C(O)O-, -C(O)N(R¹³)-, -S(O)_nN(R¹³)- or -S(O)_nO-;

5

R¹² and R¹³ independently represent, on each occasion when used above:

(A) hydrogen; or

(B) C₁₋₆ alkyl, optionally substituted by one or more substituents selected from halo, -N(R¹⁴)R¹⁵, -OR¹⁵ and =O;

10

n represents, on each occasion when used above, 1 or 2;

R³ and R⁴ independently represent H or C₁₋₆ alkyl optionally substituted by one or more substituents selected from halo, C₁₋₆ alkyl, cyano, -NO₂, -ONO₂, -N(R¹⁴)R¹⁵, -OR¹⁵, =O, aryl and heteroaryl; and

R¹⁴ and R¹⁵ independently represent, on each occasion when used above, H or C₁₋₄ alkyl,

20 or a pharmaceutically acceptable salt thereof,

for the manufacture of a medicament for the treatment of a disease in which inhibition of the activity of a lipoxygenase, and particularly 15-lipoxygenase, is desired and/or required.

25

2. A use as claimed in Claim 1, wherein R¹ represents a phenyl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from X¹, aryl and C₁₋₆ alkyl, which alkyl group is optionally substituted by one or more groups selected from X¹.

30

3. A use as claimed in Claim 1 or Claim 2, wherein R² represents a phenyl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from X¹, a heterocyclic group and C₁₋₃ alkyl, which alkyl group is optionally substituted by X¹.

5

4. A use as claimed in any one of the preceding claims, wherein X¹ represents halo, -NO₂, -A¹-R⁵ or cyano.

10 5. A use as claimed in any one of the preceding claims, wherein A¹ represents -N(R⁶)A³-, -OA⁴- or -S(O)_nA⁵-.

6. A use as claimed in any one of the preceding claims, wherein A² represents a single bond, -O- or -N(R⁶)A⁶-.

15 7. A use as claimed in any one of the preceding claims, wherein A³ represents A⁶ or -S(O)_n-.

8. A use as claimed in any one of the preceding claims, wherein A⁴ represents A⁶.

20

9. A use as claimed in any one of the preceding claims, wherein A⁵ represents -N(R⁶)-.

25

10. A use as claimed in any one of the preceding claims, wherein A⁶ represents a single bond.

11. A use as claimed in any one of the preceding claims, wherein n represents 2.

12. A use as claimed in any one of the preceding claims, wherein R⁵ represents H, C₁₋₃ alkyl or phenyl.

13. A use as claimed in any one of the preceding claims, wherein R⁶ represents H or C₁₋₃ alkyl.

14. A use as claimed in any one of the preceding claims, wherein R³ represents H or C₁₋₃ alkyl.

10 15. A use as claimed in any one of the preceding claims, wherein R⁴ represents H or C₁₋₃ alkyl, which alkyl group is optionally substituted by one or more substituents selected from phenyl and -OR¹⁵.

15 16. A use as claimed in any one of the preceding claims, wherein R¹⁵ represents C₁₋₂ alkyl.

20 17. A use as claimed in any one of the preceding claims, wherein R¹ and/or R² represent an optionally substituted pyrrolidinyl, piperidinyl, oxindolyl, phenyl, naphthyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, pyridyl, indolyl, indolinyl, isoindolinyl, quinolinyl, 1,2,3,4-tetrahydroquinolinyl, isoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, quinolizinyl, benzofuranyl, isobenzofuranyl, chromanyl, benzothienyl, pyridazinyl, pyrimidinyl, pyrazinyl, indazolyl, benzimidazolyl, quinazolinyl, quinoxalinyl, 1,3-benzodioxolyl, benzodioxanyl, tetrazolyl, benzothiazolyl and/or indazolyl group.

25 18. A use as claimed in Claim 17, wherein R¹ and/or R² represent an optionally substituted pyrrolidinyl, piperidinyl, oxindolyl, phenyl, naphthyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, pyridyl, indolyl, indolinyl, isoindolinyl, quinolinyl, 1,2,3,4-

tetrahydroquinolinyl, isoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, quinolizinyl, benzofuranyl, isobenzofuranyl, chromanyl, benzothienyl, pyridazinyl, pyrimidinyl, pyrazinyl, indazolyl, benzimidazolyl, quinazolinyl, quinoxaliny, 1,3-benzodioxolyl and/or benzodioxanyl group.

5

19. A use as claimed in Claim 17 or Claim 18, wherein the optional substituents are selected from halo, -NO₂, cyano, C₁₋₆ alkyl (which alkyl group may be linear, branched, cyclic, part-cyclic, unsaturated and/or optionally substituted with one or more fluoro group), phenyl, pyrrolidinyl, piperidinyl, piperazinyl, tetrahydrofuranlyl, tetrahydropyranyl, morpholinyl, -OR¹⁸, -N(R¹⁸)R¹⁹, -C(O)R¹⁸, -C(O)OR¹⁸, -C(O)N(R¹⁸)R¹⁹, -S(O)_mR²⁰, -S(O)₂N(R¹⁸)R¹⁹ and/or -N(R¹⁸)S(O)₂R²⁰, wherein R¹⁸ and R¹⁹ independently represent H, phenyl or C₁₋₆ alkyl, R²⁰ represents C₁₋₄ alkyl and m represents 0, 1 or 2.

15

20. A use as claimed in Claim 19, wherein the substituents are selected from fluoro, chloro, bromo, cyano, hydroxyl, amino, -NO₂, C₁₋₄ alkyl, C₁₋₄ alkoxy, phenyl, phenoxy, trifluoromethyl, -N(H)SO₂CH₃, -SO₂NH₂, -SO₂N(CH₃)₂, -SO₂N(H)CH₃, -N(CH₃)₂ and morphoinyl.

20

21. A use as claimed in Claim 20, wherein the substituents are selected from fluoro, chloro, bromo, cyano, hydroxyl, amino, -NO₂, C₁₋₄ alkyl, C₁₋₄ alkoxy, phenyl, phenoxy, trifluoromethyl, -N(H)SO₂CH₃, -SO₂NH₂ and -SO₂N(CH₃)₂.

25

22. A use as claimed in any one of the preceding claims, wherein R¹ represents thieryl; pyrazolyl, which pyrazolyl group is substituted by one or more methyl groups or is unsubstituted; pyridyl, which pyridyl group is substituted by one or more substituents selected from bromo, chloro, methyl and hydroxyl or is unsubstituted; or phenyl, which phenyl group is

30

optionally substituted by one or more substituents selected from methyl, *t*-butyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, phenyl, hydroxyl, amino, -NO₂, -SO₂NH₂, -SO₂N(CH₃)₂, -SO₂N(H)CH₃ and -N(CH₃)₂.

5 23. A use as claimed in Claim 22, wherein R¹ represents thienyl; unsubstituted pyrazolyl; unsubstituted pyridyl; or phenyl optionally substituted by one or more substituents selected from methyl, *t*-butyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, phenyl, hydroxyl, amino, -NO₂, -SO₂NH₂ and -SO₂N(CH₃)₂.

10 24. A use as claimed in any one of the preceding claims, wherein R² represents 2-pyridyl, 4-pyridyl, 2-quinoxaliny, or phenyl, which phenyl group is optionally substituted by one or more substituents selected from methyl, phenoxy, -N(H)SO₂CH₃, methoxy, fluoro, chloro, bromo, trifluoromethyl, hydroxyl, -NO₂, -SO₂NH₂, -SO₂N(CH₃)₂, cyano, morpholinyl, -N(CH₃)₂ and ethyl.

20 25. A use as claimed in Claim 24, wherein R² represents 2-pyridyl or phenyl, which phenyl group is optionally substituted by one or more substituents selected from methyl, phenoxy, -N(H)SO₂CH₃, methoxy, fluoro, chloro, bromo, trifluoromethyl, hydroxyl, -NO₂, -SO₂NH₂ and -SO₂N(CH₃)₂.

25 26. A compound of formula I as defined in any one of Claims 1 to 25, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical, provided that, when R⁴ represents H and:

(A) R³ represents H and:

(I) R² represents phenyl, then R¹ does not represent 2-furanyl, 4-pyridyl, 3-(5-methylisooxazolyl), phenyl, or 3-nitro-, 2-

hydroxy-, 2-hydroxy-3-methyl-, 4-(phenylthio)-, 2-hydroxy-5-methyl- or 4-hydroxyphenyl;

- (II) R² represents 4-chlorophenyl, then R¹ does not represent 2-furanyl, 4-pyridyl, phenyl, or 2-hydroxy-5-methyl-, 4-hydroxy-, 2-hydroxy-3-methyl- or 2-hydroxyphenyl;
- (III) R² represents 4-methylphenyl, then R¹ does not represent 4-pyridyl, phenyl, or 3-nitro-, 2-hydroxy-5-methyl-, 4-hydroxy-, 2-hydroxy- or 4-(phenylthio)phenyl; or
- (IV) R² represents 2-furanyl or 2-benzofuranyl, then R¹ does not represent 4-pyridyl or 3-(5-methylisoxazolyl); and

(B) R³ represents methyl and:

- (1) R² represents phenyl, then R¹ does not represent N-(4-bromophenyl)-2-amino-, N-(2-methoxyphenyl)-2-amino-, N-(2-ethoxyphenyl)-2-amino-, N-(3-chlorophenyl)-2-amino-, N-(4-methylphenyl)-2-amino-, N-(3-methylphenyl)-2-amino-, N-(2-methylphenyl)-2-amino- or N-(phenyl)-2-aminophenyl; or
- (2) R² represents 4-chlorophenyl, then R¹ does not represent 4-pyridyl, phenyl, or 3-nitro-, 2-hydroxy-5-methyl-, 4-hydroxy-, 2-hydroxy- or 2-hydroxy-3-methylphenyl.

20

27. A compound as claimed in Claim 26, with the additional provisos that, when R⁴ represents H, R³ represents H and R² represents phenyl or 4-methylphenyl, then R¹ does not represent 4-(thienyl)phenyl.

25

28. A pharmaceutical formulation including a compound as defined in Claim 26 or Claim 27, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

29. A compound as defined in Claim 26 or Claim 27, or a pharmaceutically-acceptable salt thereof, with the additional provisos that, when R⁴ represents H, R² represents phenyl and:

- (a) R³ represents H, then R¹ does not represent 2-pyridyl, or 3-bromo-, 5 3,4-dimethoxy- or 2-hydroxy-5-bromophenyl; and
(b) R³ represents methyl, then R¹ does not represent 4-methoxyphenyl.

30. A use as claimed in any one of Claims 1 to 25 wherein the lipoxygenase is 15-lipoxygenase.

10

31. A use as claimed in any one of Claims 1 to 25 or 30, wherein the disease is inflammation and/or has an inflammatory component.

15

32. A use as claimed in Claim 31 wherein the inflammatory disease is asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, allergic disorders, rhinitis, inflammatory bowel disease, ulcers, inflammatory pain, fever, atherosclerosis, coronary artery disease, vasculitis, pancreatitis, arthritis, osteoarthritis, rheumatoid arthritis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, 20 psoriasis, stroke, diabetes, autoimmune diseases, Alzheimer's disease, multiple sclerosis, sarcoidosis, Hodgkin's disease or another malignancy.

25

33. A method of treatment of a disease in which inhibition of the activity of a lipoxygenase is desired and/or required, which method comprises administration of a therapeutically effective amount of a compound of formula I as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, to a patient suffering from, or susceptible to, such a condition.

30

34. A combination product comprising:

- (A) a compound of formula I, as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof; and
- (B) another therapeutic agent that is useful in the treatment of inflammation,
- 5 wherein each of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

35. A pharmaceutical formulation including a compound of formula I as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, another therapeutic agent that is useful in the treatment of inflammation, and a pharmaceutically-acceptable adjuvant, diluent or carrier.

36. A kit of parts comprising components:

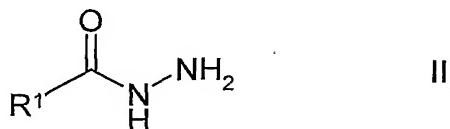
15 (a) a pharmaceutical formulation including a compound of formula I as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier; and

(b) a pharmaceutical formulation including another therapeutic agent that is useful in the treatment of inflammation in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier,

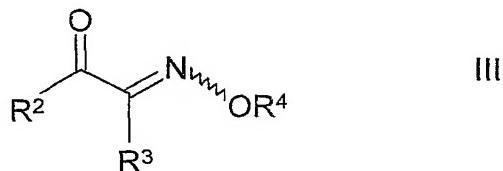
20 which components (a) and (b) are each provided in a form that is suitable for administration in conjunction with the other.

25 37. A process for the preparation of a compound as defined in Claim 29, which comprises:

- (i) reaction of a compound of formula II,

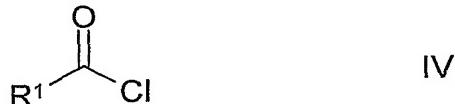


wherein R¹ is as defined in Claim 1, or an acid addition salt thereof, with a compound of formula III,

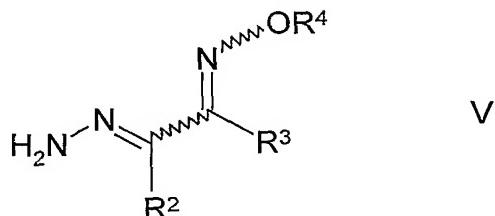


wherein the squiggly bond, R², R³ and R⁴ are as defined in Claim 1;

- 5 (ii) reaction of a compound of formula IV,

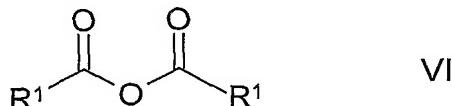


wherein R¹ is as defined in Claim 1 with a compound of formula V,



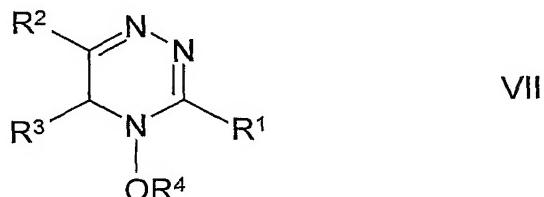
wherein the squiggly bonds, R², R³ and R⁴ are as defined in Claim 1;

- 10 (iii) reaction of a compound of formula VI,



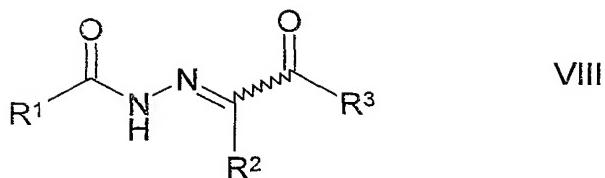
wherein R¹ is as defined in Claim 1 with a compound of formula V as defined above;

- (iv) ring opening of a compound of formula VII,

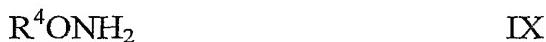


15 wherein R¹, R², R³ and R⁴ are as defined in Claim 1;

- (v) reaction of a compound of formula VIII,



wherein the squiggly bond, R¹, R² and R³ are as defined in Claim 1 with a compound of formula IX,



5 wherein R⁴ is as defined in Claim 1, or an acid addition salt thereof;

(vi) for compounds of formula I in which R⁴ represents optionally substituted C₁₋₆ alkyl, reaction of a corresponding compound of formula I in which R⁴ represents H with a compound of formula X,



10 wherein L¹ is a suitable leaving group and R^{4a} is C₁₋₆ alkyl optionally substituted by one or more substituents selected from halo, C₁₋₆ alkyl, cyano, -NO₂, -ONO₂, -N(R¹⁴)R¹⁵, -OR¹⁵, =O, aryl or heteroaryl; or

(vii) reaction of a compound of formula XI,



15 wherein L² is a suitable leaving group and R¹ is as defined in Claim 1 with a compound of formula V as defined above in the presence of carbon monoxide or another suitable CO source.